

This Week's Citation Classic

Lassen N A. Cerebral blood flow and oxygen consumption in man. *Physiol. Rev.* 39:183-238, 1959.
[Lab. Clin. Sci., National Institute of Mental Health, National Institutes of Health, Bethesda, MD]

The concept of autoregulation of cerebral blood flow was presented in detail for the first time. The paper also summarizes the field in general and contains a thorough discussion of the methods that, at that time, were available to study CBF and CMRO, in man. [The *SCI*® indicates that this Paper has been cited over 480 times since 1961.]

Niels A. Lassen
Department of Clinical Physiology
Bispebjerg Hospital
2400-Copenhagen NV
Denmark

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"This review's most lasting contribution to the understanding of cerebral circulation, and the reason for its frequent citation, is perhaps the section on *autoregulation of cerebral blood flow*: the fact that normally the cerebral vessels constrict when the blood pressure increases and dilate when the pressure decreases. Basic animal experiments showing this regulatory mechanism had been made by Mogens Fog in the 1930s.¹ However, undoubtedly due to the ease with which the autoregulation is abolished by trauma or transient hypoxia, many other workers had been unable to demonstrate it. In my article, support for the autoregulation of CBF was adduced by collecting several series of studies of induced hyper and hypotension in man, showing that within limits (and with unchanged arterial pCO₂) CBF was in fact unchanged. Why were the studies in man so uniformly effective in showing the autoregulation? I think the answer is simply that in man you must employ techniques that are essentially atraumatic.

"The data collected in the 1959 review also included several series of studies in patients with *essential hypertension*. They were

interpreted to suggest that in this disease the autoregulatory plateau—the limits of pressures between which flow is maintained constant—is shifted toward higher pressures. The cerebral resistance vessels appeared to be adapted (hypertrophied?) to the higher pressure.

"Since then we have come to know much more about the cerebral autoregulation. Its shift in chronic hypertension has been seen quite clearly, and there has been presented evidence suggesting that it may return to the normal pressure range after prolonged effective treatment.² Of special interest is the finding of a flow increase with more marked hypertension to pressures above the 'upper limit' of autoregulation.³ This flow increase and the concomitant abnormal protein permeability of the blood brain barrier is probably an initiating event in *acute hypertensive encephalopathy*.

"Recently it has been demonstrated that in severe cases of traumatic brain tissue injury with edema as well as in cases of brain edema induced experimentally by cold or associated with brain tumors autoregulation of CBF is present!⁴⁻⁵ This is so, even though we know that with milder degrees of the same noxious stimuli the mechanism is, indeed abolished! This paradox was first thought to be caused by a massive variation in intracranial pressure in the 'worst' cases. Now it appears that this is not always the case and local variations in brain tissue pressure are then invoked to explain the 'false autoregulation.' Perhaps this is so. But no proof of the tissue pressure hypothesis is yet at hand.

"Many other aspects of this article's concepts and facts continue to be elaborated in current research. What was then (and is now) called the metabolic regulation of cerebral blood flow is fertile ground. One can by measuring blood flow in a given area reveal if it is *active* or *inactive*. We can map the areas of the brain in animals or in man during sensory perception movements, vocalization, etc., as reviewed by Lassen, Ingvar, and Skinhøj in 1978.⁶

1. **Fog M.** The relationship between the blood pressure and the tonic regulation of the pial arteries. *J. Neurol. Psychiat.* 1:187-97, 1938.
2. **Strandgaard S.** Autoregulation of cerebral blood flow in hypertensive patients. The modifying influence of prolonged antihypertensive treatment on the tolerance to acute, drug-induced hypotension. *Circulation* 53:720-7, 1976.
3. **Strandgaard S, Mackenzie E T, Sengupta D, Rowan J O, Lassen N A & Harper A M.** Upper limit of autoregulation of cerebral blood flow in the baboon. *Circ. Res.* 34:435-40, 1974.
4. **Enevoldsen E M & Taagelytj-Jensen F.** Autoregulation and CO₂ responses of cerebral blood flow in patients with acute severe head injury. *J. Neurosurgery* 48:689-703, 1978.
5. **Palvölgyi R.** Regional cerebral blood flow in patients with intracranial tumors. *J. Neurosurgery* 31:149-63, 1969.
6. **Laasen N A, Ingvar D H & Skinhøj J E.** Brain function and blood flow. Changes in the amount of blood flowing in areas of the human cerebral cortex, reflecting changes in the activity of those areas, are graphically revealed with the aid of a radioactive isotope. *Sci. Amer.* 239:62-71, 1978.